

### **REMARKS**

Claims 1-7, 17, and 18 were previously pending. By this Amendment claims 1 and 18 are currently amended, no claims are canceled, and new claims 98-102 are added. No new subject matter has been introduced. Upon entry of this Amendment, claims 1-7, 17, 18, and 98-102 are pending for examination.

Claim 1 is currently amended to specify that the allergic condition other than asthma is not eczema.

Claim 18 is currently amended to delete "to the subject having an allergic condition other than asthma" and "to treat the allergic condition". This amendment is made only for purposes of improved clarity and does not alter the scope of what is claimed.

New claims 98-102 depend from claim 1 and specify particular allergic conditions other than asthma. Basis for these claims can be found, for example, at page 12, lines 13-16 of the specification.

#### **Claim Rejections Under 35 U.S.C. 112, First Paragraph – Enablement**

Claims 1-7 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. According to the Examiner, the specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation. The Examiner indicated the Wands factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art, and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. See Office Action, page 4. For reasons below, Applicant respectfully requests reconsideration.

On page 4 of the Office Action the Examiner asserts that the specification does not disclose any examples of PSA1 being used to treat any allergic disease other than asthma in any

patient. The Examiner asserts that different allergic diseases have different responses, affect [sic] different people and have different etiologies. The Examiner also acknowledges that the specification teaches that zwitterionic polysaccharides of the invention activate CD4+ T cells to produce Th1 cytokines IL-2, IFN-gamma, and IL-10, but then goes on to assert that skewing toward a Th1 response and producing IFN-gamma may not be therapeutic for all allergic diseases. (See Office Action, page 5). Later in the Office Action, however, the Examiner relies on the teachings of Tang et al. (2001) *J. Immunol.* 166:1471-81 for the proposition that allergic inflammation is a Th2-mediated disease and that an immune switch to Th1 can protect against Th2-mediated allergic responses, in support of rejections made under 35 U.S.C. 103 (see below). This reliance on Tang et al. by the Examiner would suggest that the Examiner is taking inconsistent positions in respect of the ability of Th1 cytokines to treat allergic diseases.

Applicant respectfully submits that allergic diseases, despite their differences, are complex biological phenomena that are widely recognized to share certain common underlying features, namely, a skewing toward a Th2 character at least in their initial phase of disease. As allergic diseases become more chronic, they can evolve to have more of a Th1 character. In any case, if the initial Th2 phase can be treated, then allergy and evolution toward more Th1 character can be averted. In addition, treatments that dampen both Th2 and Th1 immune responses are, not surprisingly, described to be effective for treating allergic diseases. Studies relating to the administration or neutralization of individual cytokines are generally not particularly instructive because allergic diseases are the outward manifestations of both cooperative and competing immune responses involving a wide array of cell types and signals.

On page 5 of the Office Action the Examiner points to the teachings of Hertl et al. (2000) *Allergy* 55:108-15 for the proposition that nickel allergic individuals have exhibited Th1, Th2, and Th0-type cells producing both Th1 and Th2 cytokines during the course of allergic disease. The mere observation, however, that there may be Th1 and Th0 cells, in addition to Th2 cells, or that there may be Th1 cytokines, in addition to Th2 cytokines, in an allergic disease does not necessarily mean that the skewing of an immune response toward Th1 may not be effective for treating the allergic disease. In addition, the instant disclosure also teaches that the polymers of

the invention induce proliferation of T regulatory cells (see, for example, page 23 of the specification), and such T regulatory cells are further disclosed to downregulate an immune response. Such downregulation would affect Th1, Th2, and Th0 cells. Accordingly, the teachings of Hertl et al. do not support the suggestion by the Examiner that the claimed invention is unpredictable.

The teachings of Gonzalez-Hernandez et al. (2007) *Scand. J. Immunol.* 65:368-75, cited by the Examiner, merely point out that a certain subset of T cells, which represent less than 20 percent of circulating T cells, secrete IFN-gamma, the hallmark Th1 cytokine, in acute asthma attacks. Such an observation does not, however, necessarily negate the significance of skewing an immune response toward Th1 in order to treat an allergic disease. Neither does it negate the significance of inducing T regulatory cells in order to treat an allergic disease. Accordingly, the teachings of Gonzalez-Hernandez et al. do not support the suggestion by the Examiner that the claimed invention is unpredictable.

Also on page 5 of the Office Action the Examiner cites Mamessier et al. (2006) *Eur. J. Dermatol.* 16:103-13 for the proposition that trying to alter the Th1/Th2 balance to treat allergy is not straight-forward. While Mamessier et al. does teach that targeting Th2 cytokines for allergic therapy has been inconsistent, such teaching is not relevant because it is limited to anti-IL-4 antibodies, anti-IL-5 antibodies, and anti-IL-5 receptor antibodies. The claimed invention is not so limited, and in fact Mamessier et al. goes on to teach both that Th1 induction and IL-10-producing cells (T regulatory cells) are preferred methods for treating allergic diseases. (See pages 109-111 of that reference.) Accordingly, the teachings of Gonzalez-Hernandez et al. do not support the suggestion by the Examiner that the claimed invention is unpredictable.

At the bottom of page 5 of the Office Action the Examiner asserts that the specification does not disclose adequate support for any isolated polymer which comprises repeating units of a charge motif characteristic of *B. fragilis* polysaccharide A (PSA). The Examiner cites Kalka-Moll et al. (2000) *J. Immunol.* 164:719-24 for the proposition that the recited polymer encompasses species that would not work in the claimed invention. Applicant wishes to point

out in response that not every possible embodiment is required to work in order to satisfy the enablement requirement. In addition, the specification not only includes detailed disclosure of a number of polymers that are useful (see, for example, pages 39 – 44) but also incorporates by reference the teachings of U.S. Pat. Nos. 5,679,654 and 5,700,787, as well as published international patent applications WO 96/07427, WO 00/59515, and WO 02/45708, which disclose such polymers. (See page 1 of the specification.)

On page 6 of the Office Action the Examiner asserts that the term “comprising” in claim 1 widens the scope of the claim to include polymer species that include additional molecules that may impact the ability of the polymer to treat the allergic disease. While it is true that “comprising” is open language, it is standard to use such open language in claiming an invention and this cannot form the basis for an enablement rejection.

On page 7 of the Office Action the Examiner asserts that there is a great degree of unpredictability in the art as to how these polymers work. Applicant wishes to point out in response that knowledge of mechanism of action is not a requirement for enablement.

Also on page 7 of the Office Action the Examiner asserts that the recitation of a patient who is free of symptoms otherwise calling for treatment with the polymer is not enabled. Applicant directs the Examiner’s attention to the passage at page 13, beginning at line 17, of the specification, where a large number of other conditions that can be treated using a polymer of the invention are disclosed. These same conditions are further described in U.S. Pat. Nos. 5,679,654 and 5,700,787, as well as published international patent applications WO 96/07427, WO 00/59515, and WO 02/45708, the contents of which are incorporated by reference into the disclosure of the invention.

At the bottom of page 7 of the Office Action the Examiner asserts that the term “anti-IgE” is not enabled. Applicant submits that the term “anti-IgE” plainly refers to an antibody that binds specifically to IgE, as evidenced by reference made to omalizumab (XOLAIR®, Genentech/Novartis) at page 19, lines 2-3 of the specification.

Finally, the Examiner asserts on pages 7-8 of the Office Action that the recitation of “administering comprises delivering an aerosol of the polymer to an airway of the subject” is not enabled because it is highly unpredictable that administration of the polymer to the airway of the subject will treat all allergic diseases, including contact dermatitis and food allergy. Applicant submits that aerosol delivery to an airway is an accepted method for systemic delivery of various agents. Passages on pages 32 – 36 of the specification describe how to prepare and use aerosol delivery devices to take advantage of this route of administration.

In summary, Applicant respectfully submits that the claimed invention is adequately enabled and accordingly requests that the Examiner reconsider and withdraw the rejection of claims 1-7 and 17-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

Claim Rejections Under 35 U.S.C. 112, First Paragraph – Written Description

Claims 1-7 and 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. For reasons provided below, Applicant respectfully requests reconsideration.

According to the Examiner, the specification does not adequately describe any examples of PSA1 being used to treat any allergic disease other than asthma in any patient. Applicant points out that in addition to the fact that working examples are not required, the specification discloses a representative number of different polymers, allergic diseases, dosing and routes of administration, sufficient to convey to the skilled person that Applicant in fact had possession of the claimed invention at the time the application was filed. See, for example, specification at page 12, lines 13-16 (allergic conditions); pages 1 and 39 – 44 (polymers); and pages 44 – 47 (dosing and administration).

On page 10 of the Office Action the Examiner asserts the use of the term “comprising” in claim 1 widens the scope of the claim to include polymer species that include additional molecules. Applicant submits that the disclosure makes clear that, surprisingly, specific but

rather minimal structural requirements are sufficient to determine which polymers are useful according to the claimed method. While it is true that “comprising” is open language, it is standard to use such open language in claiming an invention and this cannot form the basis for a written description rejection as suggested by the Examiner.

On page 11 of the Office Action the Examiner asserts that the terms “polysaccharide”, “capsular polysaccharide”, “patient who is free of symptoms otherwise calling for treatment with the polymer”, and “anti-IgE” are not adequately described. For the sake of brevity, Applicant refers the Examiner to passages in the specification pointed out above in connection with these terms as raised in the enablement rejection. Applicant respectfully submits these terms are adequately described.

In summary, Applicant respectfully submits that the claimed invention is adequately described and accordingly requests that the Examiner reconsider and withdraw the rejection of claims 1-7 and 17-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

#### Claim Rejections Under 35 U.S.C. 102

Claims 1-2, 4-6, and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by WO 03/075953. According to the Examiner, WO 03/075953 teaches a method for treating an allergic condition other than asthma in a subject, comprising: administering to a subject having an allergic condition other than asthma an isolated polymer in an effective amount to treat the allergic condition, wherein the polymer comprises repeating units of a charge motif characteristic of PSA, the motif being a positively charged free amino moiety and a negatively charged moiety selected from the group consisting of carboxyl, phosphonate, sulfate and sulfonate.

Without conceding to the Examiner’s position and solely in the interest of expediting prosecution, Applicant has amended claim 1 to include the limitation “wherein the allergic condition is not eczema”. Basis for this amendment can be found, for example, at page 12, lines 13-16 of the specification, where it is disclosed that allergic conditions include but are not

limited to allergic asthma, hayfever (seasonal rhinitis), allergic rhinitis, allergic conjunctivitis, eczema, urticaria, food allergies, and other atopic diseases. "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977) ('[the] specification, having described the whole, necessarily described the part remaining'.)." Applicant respectfully submits that by excluding eczema from claim 1, claim 1 is novel over WO 03/075953 because the only allergic disease other than asthma disclosed in that reference is eczema. Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-2, 4-6, and 18 under 35 U.S.C. 102(e) as being anticipated by WO 03/075953.

Claims 1-2, 4-6, and 18 are also rejected under 35 U.S.C. 102(e) as being anticipated by US 2005/0119164. US 2005/0119164 is the U.S. national phase application corresponding to WO 03/075953. For the same reasons as provided above in connection with WO 03/075953, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-2, 4-6, and 18 under 35 U.S.C. 102(e) as being anticipated by US 2005/0119164.

#### Claim Rejections Under 35 U.S.C. 103

Claims 1-7 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/59515 in view of Tang et al. (2001) *J. Immunol.* 166:1471-1481. According to the Examiner, WO 00/59515 teaches a method for treating a Th1 cell responsive disorder in a subject, comprising: administering to a subject having a Th1 cell responsive disorder an isolated polymer in an effective amount to treat the allergic condition, wherein the polymer comprises repeating units of a charge motif characteristic of PSA, the motif being a positively charged free amino moiety and a negatively charged moiety selected from the group consisting of carboxyl, phosphonate, sulfate and sulfonate. Further, according to the Examiner, Tang et al. teaches that allergic inflammation is a Th2-mediated disease and that an immune switch to Th1 can protect against Th2-mediated allergic responses. Finally, according to the Examiner, a person of ordinary skill in the art would have been motivated to apply the method of treating a Th1 cell responsive disorder of WO 00/59515 to treat the allergic airway inflammation of Tang et al.

because of Tang et al. teaches that an immune switch from a Th2 response to a Th1 response can protect against allergic airway inflammation.

Applicant respectfully requests reconsideration. WO 00/59515 does not teach or suggest Th2 to Th1 switching. Instead, WO 00/59515 teaches what is common among many immune stimulatory molecules, that is, that the polymers disclosed in WO 00/59515 induce the production of both Th1 and Th2 cytokines. The mere presence of both Th1 and Th2 cytokines is not an indication that one or the other will be favored.

WO 00/59515 teaches at page 26, lines 20-30, that the polymers induce IL-10. As stated, IL-10 “is considered to be a key Th2 cytokine which is known to inhibit Th1 function.” WO 00/59515 also teaches, as cited by the Examiner, that the polymers induce IL-2, which is a Th1 cytokine, and therefore may be used to treat Th1-responsive disorders. WO 00/59515 does not, however, suggest that the polymers will cause a predominant Th1 cytokine response and a Th2 to Th1 shift.

Tang et al. teaches that macrophages in the lung are responsible for directing a Th1-predominant response and antagonize the Th2 response of an inhaled antigen. Tang et al. also teaches on page 1480, at the end of the first full paragraph, that IL-10 is a cytokine necessary for Th2 proliferation, suggesting that IL-10 would favor a Th2 response.

Therefore, WO 00/59515, either alone or in combination with Tang et al., does not suggest that the polymers would shift from Th2 to Th1 and be useful to treat allergy. Instead, the combination, if anything, suggests not to use the polymers of WO 00/59515 to treat allergy because of the induction by the polymers of IL-10, known in the art and taught by Tang to be responsible for Th2 stimulation.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-7 and 18 under 35 U.S.C. 103(a) as being unpatentable over WO 00/59515 in view of Tang et al.



The Examiner rejected claims 1-7 and 18 under 35 U.S.C. 103(a) as unpatentable over U.S. Patent 7,026,285 in view of Tang et al. (*supra*). Applicant respectfully requests reconsideration. The cited patent is the U.S. equivalent of WO 00/59515. The rejection should be withdrawn for the same reasons as discussed above in connection with WO 00/59515.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1-7 and 18 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 7,026,285 in view of Tang et al.

Claims 1 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent Publication No. 2005/0119164 in view of Thomas et al. (2002) *BMJ* 324:1-7. According to the Examiner, it would have been obvious to one of ordinary skill in the art to apply the method of administering glucocorticoids to treat eczema of Thomas et al. to the method for treating allergic condition other than asthma in a subject including eczema in US 2005/0119164. Applicant respectfully requests reconsideration.

Claim 1, as noted above, is currently amended to exclude eczema. Apart from eczema and asthma, conditions disclosed in US 2005/0119164 are not allergic conditions other than asthma. Accordingly, there would be no reason to combine the references as suggested by the Examiner because the suggested combination does not result in the claimed invention of claim 1. Claim 17 depends from claim 1 and adds the limitation that the claimed method further includes administering to the subject an anti-allergy medicament selected from glucocorticoids, antihistamines, and anti-IgE. Since claim 17 includes all the limitations of claim 1, it too excludes eczema. Accordingly there would be no reason to combine the references as suggested by the Examiner because the suggested combination does not result in the claimed invention of claim 17.

In addition to there being no reason to combine the references as suggested by the Examiner, there would be no motivation to do so. Paragraph 0010 of US 2005/0119164 teaches that the inventors for that application

have also surprisingly discovered that when human peripheral blood mononuclear cells (PBMCs) are treated in vitro with an SPA as disclosed herein, the response is most notably the expression of IL10. Only minimal and early expression of IL2, IFN- $\gamma$ , or TNF- $\alpha$  is observed.

In other words, a person of ordinary skill in the art would understand from this passage that US 2005/0119164 teaches that the compounds and methods of that reference would favor a Th2 response. Since a Th2 response would not be expected to be desirable in treating an allergic response, there would be no motivation to combine the teachings of US 2005/0119164 with the teachings of Thomas et al., with any reasonable expectation of success.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of claims 1 and 17 under 35 U.S.C. 103(a) as being unpatentable over US Patent Publication No. 2005/0119164 in view of Thomas et al.

**CONCLUSION**

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the application in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: NOV. 16, 2007

Respectfully submitted,

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